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PS216.

Zizimin1 Overexpression Impairs Vascular Morphogenesis

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Objectives: The Rho subfamily of small GTPases, including RhoA, Rac1, and Cdc42, regulates diverse cellular functions, including polarity, migration, and actin-based cytoskeleton dynamics. Our prior studies established an essential role for Cdc42 in vascular network assembly, demonstrating that the genetic inactivation of Cdc42 yields defective vascular morphogenesis due to impaired migration of endothelial precursor cells. We have further shown that protein kinase Ciota and glycogen synthase kinase-3β are downstream effectors of Cdc42 and are involved in mediating vascular network assembly. However, the guanine nucleotide exchange factors (GEFs) that activate Cdc42, remain unknown.

Methods: We performed affinity pulldown assays using a nucleotide-free Cdc42 G15A mutant that specifically binds to Cdc42 GEFs. Mass spectrometric analysis identified Zizimin1, an upstream regulatory protein, as a candidate Cdc42 GEF.

Results: During vasculogenesis in embryoid bodies (EBs) differentiated from embryonic stem cells, Zizimin1 is highly expressed in aggregated endothelial cell precursors before vascular network formation. Surprisingly, stable overexpression of Zizimin1 in EBs resulted in the inhibition of blood vessel formation compared with control, evidenced by immunohistochemistry demonstrating loss of vascular network development. Affinity pulldown assay helped to elucidate that overexpression of Zizimin1 increases Cdc42 activity; however, the activation of Rac1 and RhoA is significantly inhibited.

Conclusions: Because Rac1 and RhoA signaling has been reported to play an essential role in embryonic blood vessel formation, our results suggest that the interplay between Rho GTPases guides vascular network assembly during development. Furthermore, these findings provide novel insights into the mechanisms of embryonic vasculogenesis and also important new information for the design of potential proangiogenic and/or antiangiogenic therapies.

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C8j: Poster Session—Research (2)

PS218.

Plasma and Patterning: The New Focus for the Development of Nanocomposite Vascular Grafts

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Objectives: The concept of surface modulation holds much promise for the future development of vascular grafts. Our aim is to enhance a nanocomposite material using surface modification techniques, such as plasma technology and surface patterning, to augment both surface chemistry and topography with a view towards endothelialization.

Methods: Polyhedral oligomeric silsesquioxane (POSS) was combined with polycarbonate urea urethane (PCU) to produce a nanocomposite polymer. Microgrooves with pitch size of 25 μm were created using photolithography. Fidelity was verified with scanning electron microscopy (SEM) and atomic force microscopy (AFM). The polymer was then exposed to pure O_2 plasma and contact angles were measured. Human umbilical vein endothelial cells (HUVECs) were then seeded onto POSS-PCU. The metabolic activity of the cells was assessed, and immunostaining was used and subsequently visualized with confocal microscopy.

Results: Contact angle results (mean, 85°) show the increased hydrophilicity of the polymer surface. Both AFM and SEM confirm the high replication fidelity of the microgrooves within the surface of the polymer using photolithography. Metabolic activity of HUVECs on the surface modified polymer was significantly increased compared with control ($P < .05$). Further immunostaining confirms the adhesive nature of the cells as well as the migratory potential.

Conclusions: A combination of plasma technology and surface patterning to augment both surface chemistry and topography on a nanocomposite polymer promotes increased endothelial cell adhesion, migration, and proliferation. The ordered microgrooves were seen to enhance cellular adhesion and spreading. Plasma technology and microgrooving is a promising methodology to optimize luminal endothelization and the prospect for "self-endothelization."

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PS220.

Quantitative In Vitro Model for the Study of Bacterial Attachment on Vascular Conduits

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Objectives: Despite prophylactic antibiotics and aseptic technique, prosthetic graft infections continue to cause significant morbidity and mortality. In contemporary reports, in vivo models have tested a conduit's infectability using concentrations from 104 to 109 colony-forming units (CFU) per mL. Using an in vitro model, we evaluated the impact of inoculation concentrations on prosthetic graft attachment.